

<!--StartFragment-->RESULT 1
US-08-690-102A-4
; Sequence 4, Application US/08690102A
; Patent No. 5789554
; GENERAL INFORMATION:
; APPLICANT: LEUNG, Shui-on
; APPLICANT: HANSEN, Hans
; TITLE OF INVENTION: IMMUNOCONJUGATES AND HUMANIZED
; TITLE OF INVENTION: ANTIBODIES SPECIFIC FOR B-CELL LYMPHOMA AND LEUKEMIA CELLS
; NUMBER OF SEQUENCES: 21
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Foley & Lardner
; STREET: 3000 K Street, N.W., Suite 500
; CITY: Washington, D.C.
; COUNTRY: USA
; ZIP: 20007-5109
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/690,102A
; FILING DATE: 01-JUL-1996
; CLASSIFICATION: 424
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: US 08/289,576
; FILING DATE: 12-AUG-1994
; ATTORNEY/AGENT INFORMATION:
; NAME: SAXE, Bernhard D.
; REGISTRATION NUMBER: 28,665
; REFERENCE/DOCKET NUMBER: 18733/463/IMIN
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (202) 672-5300
; TELEFAX: (202) 672-5399
; TELEX: 904136
; INFORMATION FOR SEQ ID NO: 4:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 116 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-690-102A-4

Query Match 100.0%; Score 620; DB 1; Length 116;
Best Local Similarity 100.0%;
Matches 116; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 QVQLQESGAELSKPGASVKMSCKASGYTFTSYWLHWIKQRPGQGLEWIGYINPRNDYTEY 60
||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Rb 1 QVQLQESGAELSKPGASVKMSCKASGYTFTSYWLHWIKQRPGQGLEWIGYINPRNDYTEY 60

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<!--StartFragment-->RESULT 1
US-08-690-102A-2
; Sequence 2, Application US/08690102A
; Patent No. 5789554
; GENERAL INFORMATION:
; APPLICANT: LEUNG, Shui-on
; APPLICANT: HANSEN, Hans
; TITLE OF INVENTION: IMMUNOCONJUGATES AND HUMANIZED
; TITLE OF INVENTION: ANTIBODIES SPECIFIC FOR B-CELL LYMPHOMA AND LEUKEMIA CELLS
; NUMBER OF SEQUENCES: 21
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Foley & Lardner
; STREET: 3000 K Street, N.W., Suite 500
; CITY: Washington, D.C.
; COUNTRY: USA
; ZIP: 20007-5109
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/690,102A
; FILING DATE: 01-JUL-1996
; CLASSIFICATION: 424
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: US 08/289,576
; FILING DATE: 12-AUG-1994
; ATTORNEY/AGENT INFORMATION:
; NAME: SAXE, Bernhard D.
; REGISTRATION NUMBER: 28,665
; REFERENCE/DOCKET NUMBER: 18733/463/IMIN
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (202)672-5300
; TELEFAX: (202)672-5399
; TELEX: 904136
; INFORMATION FOR SEQ ID NO: 2:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 113 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-690-102A-2

Query Match 100.0%; Score 589; DB 1; Length 113;
Best Local Similarity 100.0%;
Matches 112; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DIQLTQSPLAVSAGENVTMSCKSSQSVLYSANHKNYLAWYQQKPGQSPKLLIYWASTR 60
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Ph 1 DIQLTQSPLAVSAGENVTMSCKSSQSVLYSANHKNYLAWYQQKPGQSPKLLIYWASTR 60

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<!--StartFragment-->RESULT 1
AAO27198
ID AAO27198 standard; protein; 123 AA.
XX
AC AAO27198;
XX
DT 17-SEP-2003 (first entry)
XX
DE Murine anti-CD22 antibody, RFB4, VH protein.
XX
KW Framework-patching; complementarity determining region; CDR; mouse;
KW murine; cytostatic activity; cancer; Non-Hodgkin's lymphoma;
KW gene therapy; rheumatoid arthritis; FR-patching; RFB4 VH; CD22; antibody.
XX
OS Mus sp.
XX
FH Key Location/Qualifiers
FT Domain 31. .35
FT Domain /note= "Complementarity determining region (CDR) 1"
FT Domain 50. .66
FT Domain /note= "Complementarity determining region (CDR) 2"
FT Domain 99. .112
FT Domain /note= "Complementarity determining region (CDR) 3"
XX
PN WO2003002607-A1.
XX
PD 09-JAN-2003.
XX
PF 10-JUN-2002; 2002WO-US018512.
XX
PR 27-JUN-2001; 2001US-00892613.
XX
PA (LEUN/) LEUNG S S.
XX
PI Leung SS;
XX
DR WPI; 2003-210245/20.
XX
PT New re-engineered or framework-patched immunoglobulin, useful for
PT preparing a composition for treating cancer, preferably Non-Hodgkin's
PT lymphoma or rheumatoid arthritis.
XX
PS Example 1; Fig 1a; 66pp; English.
XX
CC The invention relates to a novel re-engineered or framework (FR)-patched
CC immunoglobulin, containing the heavy and/or light chain variable region
CC (VH/VL) sequences from a parent antibody. Within these chains, at least
CC one of the compartmentalised framework sequences, defined as FR1, FR2,
CC FR3 and FR4 are replaced, or patched, by the corresponding framework
CC sequences from the heavy and light chain immunoglobulin region of a
CC different species. The FR-patched immunoglobulin binds specifically to an
CC antigen with affinity comparable to, or within 3-fold of, that of the
CC parent immunoglobulin. The invention discloses the process of FR-patching
CC which is used to generate re-engineered immunoglobulin chains having one
CC or more complementarity determining regions (CDR's) from a donor
CC immunoglobulin and portions of framework sequences from one or more human
CC or primate immunoglobulins. The molecules obtained demonstrate cytostatic
CC activity as well as reduced or eliminated immunogenicity, whilst
CC maintaining the specificity and affinity of the parent antibody. The FR-
CC patched immunoglobulin is useful during the preparation of a composition
CC for treating cancer, preferably Non-Hodgkin's lymphoma and also during
CC the treatment of rheumatoid arthritis. Furthermore, the molecules of the
CC invention may also prove useful in gene therapy. The current sequence is
CC that of the murine anti-CD22 antibody, RFB4, VH protein of the invention

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XX
SQ  Sequence 123 AA;

Query Match           100.0%;  Score 648;  DB 1;  Length 123;
Best Local Similarity 100.0%;
Matches 123;  Conservative 0;  Mismatches 0;  Indels 0;  Gaps 0;

Qy      1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60
        ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||| |
Db      1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Qy      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGGSSYGVLFAYWGQGTIVT 120
        ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||| |
Db      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGGSSYGVLFAYWGQGTIVT 120

Qy      121 VSA 123
        |||
Db      121 VSA 123

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<!--EndFragment-->

<!--StartFragment-->RESULT 4
AAO27199
ID AAO27199 standard; protein; 107 AA.
XX
AC AAO27199;
XX
DT 17-SEP-2003 (first entry)
XX
DE Murine anti-CD22 antibody, RFB4, VL protein.
XX
KW Framework-patching; complementarity determining region; CDR; mouse;
KW murine; cytostatic activity; cancer; Non-Hodgkin's lymphoma;
KW gene therapy; rheumatoid arthritis; FR-patching; RFB4 VL; CD22; antibody.
XX
OS Mus sp.
XX
FH Key Location/Qualifiers
FT Domain 24. .34
FT /note= "Complementarity determining region (CDR) 1"
FT Domain 50. .56
FT /note= "Complementarity determining region (CDR) 2"
FT Domain 89. .97
FT /note= "Complementarity determining region (CDR) 3"
XX
PN WO2003002607-A1.
XX
PD 09-JAN-2003.
XX
PF 10-JUN-2002; 2002WO-US018512.
XX
PR 27-JUN-2001; 2001US-00892613.
XX
PA (LEUN/) LEUNG S S.
XX
PI Leung SS;
XX
DR WPI; 2003-210245/20.
XX
PT New re-engineered or framework-patched immunoglobulin, useful for
PT preparing a composition for treating cancer, preferably Non-Hodgkin's
PT lymphoma or rheumatoid arthritis.
XX
PS Example 1; Fig 1b; 66pp; English.
XX
CC The invention relates to a novel re-engineered or framework (FR)-patched
CC immunoglobulin, containing the heavy and/or light chain variable region
CC (VH/VL) sequences from a parent antibody. Within these chains, at least
CC one of the compartmentalised framework sequences, defined as FR1, FR2,
CC FR3 and FR4 are replaced, or patched, by the corresponding framework
CC sequences from the heavy and light chain immunoglobulin region of a
CC different species. The FR-patched immunoglobulin binds specifically to an
CC antigen with affinity comparable to, or within 3-fold of, that of the
CC parent immunoglobulin. The invention discloses the process of FR-patching
CC which is used to generate re-engineered immunoglobulin chains having one
CC or more complementarity determining regions (CDR's) from a donor
CC immunoglobulin and portions of framework sequences from one or more human
CC or primate immunoglobulins. The molecules obtained demonstrate cytostatic
CC activity as well as reduced or eliminated immunogenicity, whilst
CC maintaining the specificity and affinity of the parent antibody. The FR-
CC patched immunoglobulin is useful during the preparation of a composition
CC for treating cancer, preferably Non-Hodgkin's lymphoma and also during
CC the treatment of rheumatoid arthritis. Furthermore, the molecules of the
CC invention may also prove useful in gene therapy. The current sequence is
CC that of the murine anti-CD22 antibody, RFB4, VL protein of the invention

XX

SQ Sequence 107 AA;

Query Match 99.5%; Score 559; DB 1; Length 107;
Best Local Similarity 99.1%;
Matches 106; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DIQMTQTTSSLASLGDRVТИSCRASQDISNYLNWYQQKPDGTVKLLIYYTSILHSGVPS 60
Db 1 DIQMTQTTSSLASLGDRVТИSCRASQDISNYLNWYQQKPDGTVKLLIYYTSILHSGVPS 60

Qy 61 KFSGSGSGTDYSLTISNLEQEDFATYFCQQGNTLPWTFGGGTKLEIK 107
Db 61 RFSGSGSGTDYSLTISNLEQEDFATYFCQQGNTLPWTFGGGTKLEIK 107

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